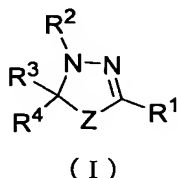


What is claimed is:

1. An antitumor agent comprising a thiadiazoline derivative represented by the general formula (I), or a pharmacologically acceptable salt thereof as an active ingredient:



<wherein Z represents a sulfur atom or -S(=O)-, R<sup>1</sup> represents substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted aryl, a substituted or unsubstituted aromatic heterocyclic group, or -C(=W)R<sup>5</sup> {wherein W represents an oxygen atom or a sulfur atom, and R<sup>5</sup> represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, -YR<sup>6</sup> (wherein Y represents an oxygen atom or a sulfur atom, and R<sup>6</sup> represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group), or -NR<sup>7</sup>R<sup>8</sup> [wherein R<sup>7</sup> and R<sup>8</sup> are the same or different, and represent a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, a substituted or unsubstituted heterocyclic group, -OR<sup>9</sup> (wherein R<sup>9</sup> has the same meaning as that of the aforementioned R<sup>6</sup>), or -NR<sup>10</sup>R<sup>11</sup> (wherein R<sup>10</sup> and R<sup>11</sup> are the same or different, and represent a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group, or R<sup>10</sup> and R<sup>11</sup> are combined together with the adjacent nitrogen atom to form a substituted or unsubstituted heterocyclic group), or R<sup>7</sup> and R<sup>8</sup> are combined together with the adjacent nitrogen atom to form a substituted or unsubstituted heterocyclic group}},

R<sup>2</sup> represents a hydrogen atom, substituted or unsubstituted lower alkyl, or -C(=W<sup>1</sup>)R<sup>12</sup> [wherein W<sup>1</sup> represents an oxygen atom or a sulfur atom, R<sup>12</sup> represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, a substituted or unsubstituted heterocyclic group, -Y<sup>1</sup>R<sup>13</sup> (wherein Y<sup>1</sup> represents an oxygen atom or a sulfur atom, and R<sup>13</sup> represents substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group), or -NR<sup>14</sup>R<sup>15</sup> (wherein R<sup>14</sup> and R<sup>15</sup> are the same or different, and represent a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group, or R<sup>14</sup> and R<sup>15</sup> are combined together with the adjacent nitrogen atom to form a substituted or unsubstituted heterocyclic group)],

R<sup>3</sup> represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group, and

R<sup>4</sup> represents substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group,

or R<sup>3</sup> and R<sup>4</sup> are combined together to represent

-(CR<sup>16A</sup>R<sup>16B</sup>)<sub>m1</sub>-Q-(CR<sup>16C</sup>R<sup>16D</sup>)<sub>m2</sub> {wherein Q represents a single bond, substituted or unsubstituted phenylene, or cycloalkylene, m1 and m2 are the same or different, and each represents an integer of 0 to 4, with the proviso that m1 and m2 are not 0 at the same time,

R<sup>16A</sup>, R<sup>16B</sup>, R<sup>16C</sup> and R<sup>16D</sup> are the same or different, and represent a hydrogen atom, halogen, substituted or unsubstituted lower alkyl, -OR<sup>17</sup> [wherein R<sup>17</sup> represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted

or unsubstituted cycloalkyl, substituted or unsubstituted aryl, a substituted or unsubstituted heterocyclic group,  $-\text{CONR}^{18}\text{R}^{19}$  (wherein  $\text{R}^{18}$  and  $\text{R}^{19}$  are the same or different, and represent a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group, or  $\text{R}^{18}$  and  $\text{R}^{19}$  are combined together with the adjacent nitrogen atom to form a substituted or unsubstituted heterocyclic group),

$-\text{SO}_2\text{NR}^{20}\text{R}^{21}$  (wherein  $\text{R}^{20}$  and  $\text{R}^{21}$  have the same meanings as those of the aforementioned  $\text{R}^{18}$  and  $\text{R}^{19}$ , respectively), or  $-\text{COR}^{22}$  (wherein  $\text{R}^{22}$  represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group)],  $-\text{NR}^{23}\text{R}^{24}$  [wherein  $\text{R}^{23}$  and  $\text{R}^{24}$  are the same or different, and represent a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, a substituted or unsubstituted heterocyclic group,  $-\text{COR}^{25}$  (wherein  $\text{R}^{25}$  represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, a substituted or unsubstituted heterocyclic group, substituted or unsubstituted lower alkoxy, substituted or unsubstituted aryloxy, amino, substituted or unsubstituted lower alkylamino, di-(substituted or unsubstituted lower alkyl)amino, or substituted or unsubstituted arylamino), or  $-\text{SO}_2\text{R}^{26}$  (wherein  $\text{R}^{26}$  represents substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group), or  $\text{R}^{23}$  and  $\text{R}^{24}$  are combined together with the adjacent nitrogen atom to form a substituted or unsubstituted heterocyclic group], or  $-\text{CO}_2\text{R}^{27}$  (wherein  $\text{R}^{27}$  represents a hydrogen atom, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted

heterocyclic group), or R<sup>16A</sup> and R<sup>16B</sup>, or R<sup>16C</sup> and R<sup>16D</sup> are combined together to represent an oxygen atom, and when m1 or m2 is an integer of 2 or more, any of R<sup>16A</sup>, R<sup>16B</sup>, R<sup>16C</sup> and R<sup>16D</sup> may be the same or different, and any two of R<sup>16A</sup>, R<sup>16B</sup>, R<sup>16C</sup> and R<sup>16D</sup> which are bound to the adjacent two carbon atoms may combine together to form a bond}>.

2. The antitumor agent according to claim 1, wherein R<sup>1</sup> is substituted or unsubstituted lower alkynyl, substituted or unsubstituted aryl, or a substituted or unsubstituted aromatic heterocyclic group.

3. The antitumor agent according to claim 1, wherein R<sup>1</sup> is substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, or -C(=W)R<sup>5</sup> (wherein W and R<sup>5</sup> have the same meanings as those mentioned above).

4. The antitumor agent according to claim 1, wherein R<sup>1</sup> is substituted or unsubstituted aryl, or a substituted or unsubstituted aromatic heterocyclic group.

5. The antitumor agent according to claim 1, wherein R<sup>1</sup> is substituted or unsubstituted aryl.

6. The antitumor agent according to claim 1, wherein R<sup>1</sup> is substituted or unsubstituted lower alkynyl.

7. The antitumor agent according to claim 1, wherein R<sup>1</sup> is substituted or unsubstituted lower alkyl, or substituted or unsubstituted lower alkenyl.

8. The antitumor agent according to any one of claims 1 to 7, wherein R<sup>2</sup> is a hydrogen atom, substituted or unsubstituted lower alkyl, or -C(=W<sup>1</sup>)R<sup>12</sup> (wherein W<sup>1</sup> and R<sup>12</sup> have the same meanings as those mentioned above, respectively).

9. The antitumor agent according to any one of claims 1 to 7, wherein R<sup>2</sup> is -C(=W<sup>1</sup>)R<sup>12</sup> (wherein W<sup>1</sup> and R<sup>12</sup> have the same meanings as those mentioned above, respectively).

10. The antitumor agent according to claim 8 or 9, wherein R<sup>12</sup> is substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, or substituted or unsubstituted cycloalkyl.

11. The antitumor agent according to claim 8 or 9, wherein R<sup>12</sup> is substituted or unsubstituted lower alkyl.

12. The antitumor agent according to claim 8 or 9, wherein R<sup>12</sup> is lower alkyl.

13. The antitumor agent according to any one of claims 8 to 12, wherein W<sup>1</sup> is an oxygen atom.

14. The antitumor agent according to any one of claims 1 to 13, wherein R<sup>3</sup> is substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group.

15. The antitumor agent according to any one of claims 1 to 13, wherein R<sup>3</sup> is substituted or unsubstituted lower alkyl.

16. The antitumor agent according to any one of claims 1 to 13, wherein R<sup>3</sup> is substituted lower alkyl.

17. The antitumor agent according to any one of claims 1 to 16, wherein R<sup>4</sup> is substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group.

18. The antitumor agent according to any one of claims 1 to 16, wherein R<sup>4</sup> is substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group.

19. The antitumor agent according to any one of claims 1 to 16, wherein R<sup>4</sup> is substituted or unsubstituted phenyl, or substituted or unsubstituted thienyl.

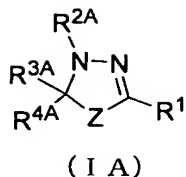
20. The antitumor agent according to any one of claims 1 to 13, wherein R<sup>3</sup> and R<sup>4</sup> are combined together to represent  $-(\text{CR}^{16\text{A}}\text{R}^{16\text{B}})_{\text{m}1}\text{-Q-}(\text{CR}^{16\text{C}}\text{R}^{16\text{D}})_{\text{m}2}$  (wherein Q, R<sup>16A</sup>, R<sup>16B</sup>, R<sup>16C</sup>, R<sup>16D</sup>, m<sub>1</sub> and m<sub>2</sub> have the same meanings as those mentioned above, respectively).

21. The antitumor agent according to any one of claims 1 to 13, wherein R<sup>3</sup> and R<sup>4</sup> are combined together to represent  $-(\text{CH}_2)_{\text{m}1}\text{-Q-}(\text{CH}_2)_{\text{m}2}$  (wherein Q, m<sub>1</sub> and m<sub>2</sub> have the same meanings as those mentioned above, respectively).

22. The antitumor agent according to claim 20 or 21, wherein Q is substituted or unsubstituted phenylene.

23. A mitotic kinesin Eg5 inhibitor comprising the thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 1 to 22 as an active ingredient.

24. A thiadiazoline derivative represented by the formula (IA) or a pharmacologically acceptable salt thereof:



{wherein Z has the same meaning as that mentioned above,

R<sup>1</sup> has the same meaning as that mentioned above,

(A) when R<sup>1</sup> is substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, or -C(=W)R<sup>5</sup> (wherein W and R<sup>5</sup> have the same meanings as those mentioned above, respectively), R<sup>2A</sup>, R<sup>3A</sup> and R<sup>4A</sup> have the same meanings as those of the aforementioned R<sup>2</sup>, R<sup>3</sup> and R<sup>4</sup> (with proviso that Z<sup>A</sup> is a sulfur atom, R<sup>1</sup> is benzyl, R<sup>2A</sup> is acetyl, one of R<sup>3</sup> and R<sup>4A</sup> is methyl, and the other of R<sup>3</sup> and R<sup>4A</sup> is not 2-oxopropyl), respectively

(B) when R<sup>1</sup> is substituted or unsubstituted lower alkynyl, or a substituted or unsubstituted aromatic heterocyclic group, R<sup>2A</sup> and R<sup>3A</sup> have the same meanings as those of the aforementioned R<sup>2</sup> and R<sup>3</sup>, respectively, and R<sup>4A</sup> represents substituted or unsubstituted aryl, or a substituted or unsubstituted heterocyclic group, and

(C) when R<sup>1</sup> is substituted or unsubstituted aryl, R<sup>2A</sup> represents -C(=W)R<sup>12</sup> (wherein W and R<sup>12</sup> have the same meanings as those mentioned above, respectively), R<sup>3A</sup> represents -(CH<sub>2</sub>)<sub>k</sub>NHSO<sub>2</sub>R<sup>3B</sup> [wherein k represents an integer of 1 to 6, and R<sup>3B</sup> represents substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkynyl, or -NR<sup>7B</sup>R<sup>8B</sup> (wherein R<sup>7B</sup> and R<sup>8B</sup> have the same meanings as those of the aforementioned R<sup>7</sup> and R<sup>8</sup>, respectively)], -(CH<sub>2</sub>)<sub>k</sub>NR<sup>7C</sup>R<sup>8C</sup> (wherein k has the same meaning as that mentioned above, and R<sup>7C</sup> and R<sup>8C</sup> have the same meanings as those of the aforementioned R<sup>7</sup> and R<sup>8</sup>, respectively), or -(CH<sub>2</sub>)<sub>k</sub>NHC(=O)R<sup>7D</sup> (wherein k has the same meaning as that mentioned above, and R<sup>7D</sup> has the same meaning as that of the aforementioned R<sup>7</sup>), and R<sup>4A</sup> has the same meaning as that of the aforementioned R<sup>4</sup>).

25. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to claim 24, wherein Z is a sulfur atom.

26. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to claim 24 or 25, wherein R<sup>1</sup> is substituted or unsubstituted lower alkynyl, substituted or unsubstituted aryl, or a substituted or unsubstituted aromatic heterocyclic group.

27. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to claim 24 or 25, wherein R<sup>1</sup> is substituted or unsubstituted aryl.

28. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to claim 24 or 25, wherein R<sup>1</sup> is substituted or unsubstituted phenyl.

29. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to claim 24 or 25, wherein R<sup>1</sup> is substituted or unsubstituted lower alkynyl.

30. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to claim 24 or 25, wherein R<sup>1</sup> is substituted lower alkyl.

31. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to claim 24 or 25, wherein R<sup>1</sup> is -C(=W)R<sup>5</sup> (wherein W and R<sup>5</sup> have the same meanings as those mentioned above, respectively).

32. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to claim 31, wherein W is an oxygen atom.

33. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to claim 31 or 32, wherein R<sup>5</sup> is -NR<sup>7</sup>R<sup>8</sup> (wherein R<sup>7</sup> and R<sup>8</sup> have the same meanings as those mentioned above, respectively).

34. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 24 to 33, wherein R<sup>2A</sup> is -C(=O)R<sup>12</sup> (wherein R<sup>12</sup> have the same meanings as those mentioned above).

35. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to claim 34, wherein R<sup>12</sup> is lower alkyl.

36. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 24 to 35, wherein R<sup>3A</sup> is substituted or unsubstituted lower alkyl.

37. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 24 to 35, wherein R<sup>3A</sup> is -(CH<sub>2</sub>)<sub>k</sub>NHSO<sub>2</sub>R<sup>3B</sup> (wherein k and R<sup>3B</sup> have the same meanings as those mentioned above, respectively), -(CH<sub>2</sub>)<sub>k</sub>NR<sup>7C</sup>R<sup>8C</sup> (wherein k, R<sup>7C</sup> and R<sup>8C</sup> have the same meanings as those mentioned above, respectively), or -(CH<sub>2</sub>)<sub>k</sub>NHC(=O)R<sup>7D</sup> (wherein k and R<sup>7D</sup> have the same meanings as those mentioned above, respectively).

38. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 24 to 35, wherein R<sup>3A</sup> is -(CH<sub>2</sub>)<sub>k</sub>NHSO<sub>2</sub>R<sup>3B</sup>

(wherein k and R<sup>3B</sup> have the same meanings as those mentioned above, respectively).

39. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 24 to 38, wherein R<sup>4A</sup> is substituted or unsubstituted aryl, or a substituted or unsubstituted aromatic heterocyclic group.

40. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 24 to 38, wherein R<sup>4A</sup> is substituted or unsubstituted aryl.

41. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 24 to 38, wherein R<sup>4A</sup> is substituted or unsubstituted phenyl, or substituted or unsubstituted thienyl.

42. The thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 24 to 38, wherein R<sup>4A</sup> is phenyl.

43. A medicament comprising the thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 24 to 42 as an active ingredient.

44. A mitotic kinesin Eg5 inhibitor comprising the thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 24 to 42 as an active ingredient.

45. A therapeutic agent for a disease involving cell proliferation comprising the thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 24 to 42 as an active ingredient.

46. An antitumor agent comprising the thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 24 to 42 as an active ingredient.

47. A method for therapeutic and/or preventive treatment of a malignant tumor which comprises administering an effective amount of the thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 1 to 22.

48. A method for inhibiting a mitotic kinesin Eg5 which comprises administering an effective amount of the thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 1 to 22.

49. Use of the thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 1 to 22 for the manufacture of an



antitumor agent.

50. Use of the thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 1 to 22 for the manufacture of a mitotic kinesin Eg5 inhibitor.

51. A method for inhibiting a mitotic kinesin Eg5 which comprises administering an effective amount of the thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 24 to 42.

52. A method for therapeutic and/or preventive treatment of a disease involving cell proliferation which comprises administering an effective amount of the thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 24 to 42.

53. A method for therapeutic and/or preventive treatment of a malignant tumor which comprises administering an effective amount of the thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 24 to 42.

54. Use of the thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 24 to 42 for the manufacture of a mitotic kinesin Eg5 inhibitor.

55. Use of the thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 24 to 42 for the manufacture of a therapeutic agent for a disease involving cell proliferation.

56. Use of the thiadiazoline derivative or a pharmacologically acceptable salt thereof according to any one of claims 24 to 42 for the manufacture of an antitumor agent.